be removed without delay, it does not follow that it is surgical apostasy to leave a fallopian tube in similar condition alone, when the accumulated experience of many years the world over has proved it to be the wiser course. The maxim *"primum non nocere"* has no greater application than in acute salpingitis.

CESAREAN SECTION

Much has been written about cesarean section—its value, indications, technique and its abuses. In regard to the latter, no subject seems to provoke more discussion in obstetric circles. Without assuming an illiberal state of mind, it must be stated that there is good reason for disapproval of the high percentage of cesareans being performed in many hospitals. We have not as yet been able to avoid the fact that this operation carries within itself a certain inescapable mortality; and, just as surely as night follows day, this must catch up with the operator sooner or later. Just as in all obstetrical procedures there are certain definite and other less well-defined indications for its performance, the sanctity of which should not be violated. The whim of the patient, in her lack of information on the subject, is not one of them. The obstetrical problem in the greater number of cases has merely begun at the time of the cesarean section: "Once a cesarean, always a cesarean," unless the informed patient elects to assume the danger lurking in a subsequent delivery through the natural passage.

Some hospitals have made it a rule that no cesarean may be performed without consultation. This has resulted in distinct reduction in the incidence of this operation, with no dire results to anyone concerned. Whether or not the universal application of this requirement would be wise or proper is open to argument, but the fact remains that some hospital staffs have resorted to it in desperation.

On the other hand some men go to the opposite extreme: there must be a formidable set of ironclad indications present before they resort to section with fear and trepidation. We have all read reports literally glowing with pride, detailing the protocols of hapless patients who, after horrendous and protracted labors and deliveries, had escaped cesarean section. It cannot be gainsaid that such reports can often show low maternal mortality statistics; but, in my opinion, while admittedly the most important, a low mortality is not the whole story. There are, after all, such things as badly torn cervices, third-degree lacerations of the perineum, increased incidence of puerperal infection and various tragic injuries to, or loss of the child which have to be taken into account. In obstetrics, there is little to choose, in my way of thinking, between that attitude which has been aptly termed "paraplegia pollyanna" and a surgical jamboree.

IN CONCLUSION

Every man who tries to practice medicine conscientiously can think of numerous other situations where the tug of war goes on between those whose approach to a given problem seems either too radical or too conservative. Each have factors in their favor at one time or another; neither is ever always right. In all cases, however, it is the patient who takes the risk. How much better, it seems to me, to try to strike a balance somewhere between radicalism and conservatism in outlook and in action; to keep an open mind, not overenthusiastic about unproven novelties, nor yet closed to progress; to avoid undue haste without becoming mired in the muck of indecision. It is my conviction that the ends of our art will best be attained if we take the middle road.

411 Thirtieth Street.

PNEUMONIA IN CHILDREN: TREATMENT WITH SULFAPYRIDINE*

By E. Earl Moody, M. D.
AND
E. G. Knouf, M. D.
Los Angeles

THIS study represents observations made on 126 cases of pneumonia in children all under fourteen years of age treated with sulfapyridine. They were observed at the Los Angeles County General Hospital from March through December of 1939. During this period there were fewer cases of pneumonia in children and the degree of severity of the disease was less as compared with former years. This fact may have had some effect on our mortality rate.

Ninety-nine of the cases included in this series were diagnosed as lobar pneumonia and twenty-seven as bronchopneumonia. Six cases, all in children under two years of age, were secondary to measles. The cases here presented comprise approximately half the total number of pneumonias seen during the period of observation. Those selected were the most toxic and some specific therapy seemed indicated. No other method of therapy was employed except those measures which were indicated for the comfort of the patient. In order to maintain uniformity in the clinical observations, all cases of pneumonia in children seen in the hospital during this period were under the direct control of the authors who were ably assisted by the interns on the service. Each patient was examined and observed by at least two of this group each day.

DIAGNOSTIC PROCEDURE

Before starting therapy on any case, the following criteria were fulfilled: (1) clinical diagnosis of severe, toxic pneumonia; (2) confirmation of the physical diagnosis by x-ray; (3) a complete blood count; (4) a urinalysis; (5) a blood culture; and (6) sputum typing. For the latter, material was obtained by swabbing the nasopharynx and larynx. If no type was obtained, this procedure was repeated three to five times. Failure to obtain a type did not defer treatment if the other criteria had been fulfilled.

DRUG DOSAGE

The twenty-four hour dosage was calculated on the basis of 1 to 1.5 grains per pound of body weight. This daily dose did not exceed 90 grains in

* Read before the Section on Pediatrics at the sixty-ninth annual session of the California Medical Association, Coronado, May 6–9, 1940.

TABLE 1.—*Age Distribution*

Age in Years	Number	Per Cent
0–1	29	23
1–2	30	24
2–4	21	17
4–8	23	18
8–14	23	18
Total	126	100

any twenty-four-hour period. The total daily dose was divided by six and given at four-hour intervals day and night. The initial amount of sulfapyridine given was double the calculated four-hour dose. The drug was given orally in all but seven cases. In the latter sulfapyridine was given per rectum. Milk was the usual vehicle. Sodium bicarbonate was not given routinely with the drug.

FOLLOW-UP PROCEDURES

The routine follow-up was: (1) daily chest examination; (2) complete blood count every twenty-four to forty-eight hours during the time of drug administration and every three days thereafter as long as the patient remained in the hospital; (3) urinalysis every three or four days; (4) x-ray taken one week after the temperature reached normal if the lungs were clinically clear, with subsequent ones as indicated, and (5) sulfapyridine blood concentration determination daily, continued one to two days after the drug was stopped. Blood for this determination was taken each morning at the same hour on all the patients.

AGES

In this study we were most concerned with the effects of this new drug on the young child suffering with pneumonia. Lobar pneumonia in children over four years of age is as a rule not seriously hazardous to life. Death rates rarely exceed 8 per cent. But that group of children under four years of age suffering with pneumonia, especially of the primary disseminated type, has a death rate often as high as 30 per cent. Table 1 shows the age distribution for the group. Eighty cases, or 64 per cent, were four years of age or under. Twenty-three per cent of the total number were under one year of age, and 23 per cent were between one and two years of age. Thus we had ample opportunity to see the effects of this drug in the age group in which pneumonia is so serious.

TABLE 3.—*Cases Showing Bacteremia*

Age	Organism		Complication	Fatality		Pneumonia
	Blood	Sputum		No.	Per Cent	Location
			(PNEUMOCOCCIC)			
0-1	I	VII	Empyema Strept. V. Staph. A.			RUL
	I	0		1	16.6	LLL
	I	I	Empyema Typ. I.			RUL
2-4	XIV	0				RUL
	I	I	Leukemoid Reaction			RUL
	XII	Strept.				LLL
Total	6			1	16.6	
			(OTHER ORGANISMS)			
1-2	Staph. Aureus	XVII				RM RLL
2-4	Para-Typhoid B	VI				LLL
Total	2					

PNEUMONIA TYPES

We were able to obtain pneumonia types in only seventy-three cases or 59 per cent. Fifteen types were found, the most common of which were Types I, VII, XIV, VI, XXIII and IV in the order given. Table 2 shows the various types found and the age groups in which they were obtained.

BACTEREMIA

Eight cases had positive blood cultures and are tabulated in Table 3. Three of these were of Type I in ages 9 months, 2½ years and 9 years. Two were Type XII in ages 9 months and 2 years. One was a Type XIV in a 2-year-old child. Two children

TABLE 2.—*Pneumococcus Types by Ages*

Ages	TYPES															Total
	I	II	III	IV	VI	VII	X XI	XII	XIII	XIV	XVII	XVIII	XIX	XXI	XXIII	
0– 1					2	4	1	1	1	3		1	1		2	16
1– 2				3	3	2			1	4	1				2	16
2– 4	3			1	3	3				1					1	12
4– 8	7	1				3				1						12
8–14	10	1	1			3		1		1			1	1		19
Total	20	2	1	4	8	15	1	2	2	10	1	1	2	1	5	75

TABLE 4.—*Estimated Duration of Disease When Drug Started*

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14
No. of Cases	10	15	29	32	12	9	6	2	5	2	0	1	1	2
Per Cent	8	12	23	24	10	7	5				11			
	77%													

showed blood cultures positive to organisms other than the pneumococcus. One 19-month infant showed Staphylococcus aureus on two consecutive blood cultures. The sputum showed Type XVII. In this case the temperature reached normal twenty-four hours after giving sulfapyridine. The lungs cleared by the fourteenth day. Treatment was stopped after three days. One boy, two years old, had two blood cultures positive for paratyphoid B. Cultures were taken at five-day intervals and the agglutination titer was 1-2560 and 1-5120, respectively. His stool cultures were negative. He was suffering with a left lower pneumonic consolidation. The sputum showed Type VI pneumococcus. The drug was continued for seven days though the temperature reached normal after four days of treatment. It did not rise again. All subsequent blood cultures were negative.

All of these patients with bacteremia made an uneventful recovery with the exception of one 9-month infant suffering from Type XII pneumococcus septicemia. Thus our mortality rate for the cases of pneumococcic bacteremia was 16.6 per cent.

DURATION OF THE DISEASE WHEN DRUG STARTED

When dealing with a disease that may end by crisis, it is possible wrongly to conclude that the rapid drop of the temperature was due to the drug used when, in fact, it was due to the normal crisis. Therefore, it is important that we have some knowledge of the duration of the disease when the drug was started. This of course could only be conjectured because we had to rely entirely on the history. Treatment as shown in Table 4 was started in 98 cases or 77 per cent by the fifth day of the disease. Thus we feel we can justly conclude that the universal early drop of the temperature to normal was due, in the vast majority of cases, to the effects of the drug and not to normal crisis.

TABLE 6.—*Time Required for Temperature to Reach Normal After Drug Started*

Day Normal	No. Cases	Per Cent	Complications	No.
1	75	59.5	Lung Abscess	1
2	31	24.6	0	
3	8	6.3	0	
4	3	2.4	0	
5	0	0	0	
6	2	1.6	0	
More than six days	6	4.8	Tuberculosis Empyema	1 5
Deaths	1	0.8	0	
Total	126	100.0		7

Table 5 shows an analysis of those twenty-nine patients sick longer than five days when the sulfapyridine was started. Since seven or 24 per cent of this number were bronchopneumonias in which the temperature is apt to be very protracted, and since in only two of the twenty-nine cases did it take longer than forty-eight hours for the temperature to reach normal, while nineteen or 66 per cent reached normal in twenty-four hours, we feel that we can also rightfully conclude that even these cases were beneficially affected by the drug.

TIME FOR TEMPERATURE TO REACH NORMAL

As stated above, one of the criteria for inclusion in this series was the severely ill child. High temperature was considered as one of the indications for the use of the drug. Eighty per cent of the group had temperatures above 103 degrees Fahrenheit, and 50 per cent above 104 degrees Fahrenheit when the drug was started. Many were above 106 degrees Fahrenheit. All temperature values are rectal.

The rapid drop of the temperature to normal was one of the spectacular effects of the drug. The time required for this to occur is visualized in Table 6. Eighty-four per cent had a normal temperature in

TABLE 5.—*Analysis of Cases Ill: Longer Than Five Days When Drug Started, Showing Diagnosis, Cases Not Typed, Time for Temperature Drop*

Days Ill	No. Cases	Type Pneumonia		No. Cases Not Typed	Temperature Normal		
		Broncho	Lobar		24 Hours	48 Hours	Longer
6	10	3	7	6	8	2	
7	6	0	6	3	3	2	1
8	2	0	2	1	1	1	
9	2	0	2	1	1	1	
10	4	1	3	2	3		1
11	1	1	0	0	1		
12	1	0	1	0	1		
13	1	1	0	0		1	
14	2	1	1	0	1	1	

TABLE 7.—*Days Received Drug*

Days	2	3	4	5	6	7	8	9	12
No. Cases	10	35	34	26	7	7	4	2	1
Per Cent	8	28	27	20	7	6	3	1	

forty-eight hours; however, in 59 per cent of the total cases this occurred in the first twenty-four hours of therapy. Those with pneumococcic bacteremia dropped as rapidly. Those cases that required longer than six days for the temperature to reach normal usually had some complication which the drug did not affect. The five cases of empyema which developed seemingly were unchanged in their course by the drug.

It was noted that with the drop in temperature a very large number—39 or 31 per cent—of the cases had subnormal levels which tended to persist for several days. Three cases had temperatures between 96 and 96.8 degrees Fahrenheit, while that of thirty-six cases ranged between 97 and 97.8 degrees Fahrenheit.

DAYS DRUG GIVEN

Table 7 shows the time the drug was given. This varied from two to twelve days. Eighty-three per cent received the drug not longer than five days. As we gained experience in this study we came to the conclusion that if the temperature did not reach normal by the fourth day, continuation of the drug would have little effect on the course of the disease. Early in the series we learned that sulfapyridine is a potent and dangerous drug; thus we concluded that long-continued administration should be avoided. If early drop in temperature did not occur, we were inclined to feel that other methods of therapy were indicated or the diagnosis should be corrected.

RESOLUTION OF LUNGS

While we have no controls to compare with this series, it is our impression that the time required for the lungs to become free of findings was not hastened by the use of sulfapyridine. The days required for the chest to clear is shown in Table 8.

It was the impression of the roentgenologist that resolution was even delayed. This he observed in the adult cases treated with sulfapyridine also. This possibility is demonstrated in the case of an infant, one month old, who entered the hospital with a right upper and right lower lobe pneumonia due to a Type XIII pneumococcus. In five days she received 50 grains of the drug. Temperature dropped to normal in forty-eight hours. She remained in the hospital fourteen days. She was discharged with an unresolved right upper consolidation but with no fever. She has been closely followed in the outpatient department and has been admitted to the hospital on two subsequent occasions because of a definite acute pneumonic process in the right upper lobe. No pneumococci have been found in the sputum since the original infection. The right upper lobe is still unresolved six months after her original entry to the hospital. She remains fever-free except during the recurrent attacks of pneumonia involving this area. Only streptococci and staphylococci have been recovered in the sputum. Repeated tuberculin skin tests have been negative. The case which developed a lung abscess (to be described later) further confirms this contention of delayed resolution.

TABLE 9.—*Ages of Children Taking Longer Than Seven Days for Complete Resolution (Empyema-Lung Abscess Excluded)*

Age in Years	Total Cases in Age Group		Delayed Resolution		
	No.	Per Cent	No.	Per Cent Age Group	Per Cent Total Cases
0–1	29	23	15	33.5	12
1–2	30	24	14	31.5	11
2–4	21	17	4	9	3
4–8	23	18	6	13	5
8–14	23	18	6	13	5
Total	126	100	45	100	36

Only 68 per cent of the cases had no chest findings by the ninth day. It is interesting to note that of the forty-five cases (36 per cent) which took longer than seven days for complete resolution to occur, thirty-three cases or 74 per cent of those showing delayed resolution occurred in children under four years of age. This observation is visualized in Table 9. Thus it would seem that age was a

TABLE 8.—*Number Days Before Chest Cleared After Therapy (Death and Complications Excluded)*

Days		2	3	4	5	6	7	8	9	10	11	12	13	14	15	24	29	30	34	Longer
No.	Lobar	3	2	10	10	13	11	9	8	9	4	5	0	3	0	1	1	1	1	1
	Bronch	1	1	4	5	2	4	0	3	2	1	2	1	0	1					
Total		4	3	14	15	15	15	9	11	11	5	7	1	3	1	1	1	1	1	1
Per Cent		3	2	11	12	12	12	7	9	9	4	5	1	2	4					1

Deaths	1
Empyema	5
Lung Abscess	1

TABLE 10.—*Blood Concentration. Rectal Therapy*

Case	Concentration Milligram Per Cent	Type	Temperature Normal	Complication	Vomiting
1	0.8—1.8	0	24 hrs.	0	0
2	1.8—7.5	0	24 hrs.	Empyema H. Strept.	0
3	2.1—3.4	III	24 hrs.	0	0
4	Tr.—4.1	IV	24 hrs.	0	0
5	Tr.—2.8	I	48 hrs.	0	0
6	3.3—8.9	I	48 hrs.	0	0
7*	1.0—4.6	VI	21 days	Tuberculosis	0

*Case 7 had rectal therapy for nine days, no treatment for three days, then oral therapy for nine days. (186 grains each period.)

Concentration Compared (Analogous days)

Oral	7.3	5.8	4.3	6.4
Rectal	1.0	2.2	5.0	2.4

factor in this delayed resolution when such children were treated with sulfapyridine.

It was consistently observed in these 126 cases that if consolidation was not massive when the drug was started such did not occur in the progress of the disease. In fact, the picture of pneumonia with which we are so familiar, changed so rapidly that it was with difficulty a sufficient number of typical cases of lobar pneumonia was found for the teaching service.

SULFAPYRIDINE BLOOD CONCENTRATION

We found the concentration of the drug in the blood stream a variable and unpredictable thing. This varied from a trace to a high of 17.9 milligrams per cent. It varied from day to day with the same dosage. Concentration was so variable that it was difficult to strike an average, but most cases varied between 4 and 8 milligrams per cent. An average of twenty-five cases picked at random showed a concentration for the first three days of therapy of 4.6, 5.0, and 4.2 milligrams per cent, respectively. The degree of concentration seemingly had little effect on the drop in temperature, coming as rapidly in weaker concentrations as in the stronger. We offer no explanation for this variability. The drug was excreted with variable speed but was usually completely eliminated in twenty-four to forty-eight hours.

The patient with the highest concentration was a 6-year-old boy. There was nothing unusual that would account for this high concentration. He had no kidney abnormality. He had a Type I pneumonia, being extremely toxic with a temperature of 106 degrees Fahrenheit at the onset of treatment. The concentration on successive days was 9.6, 14.5, and 17.9 milligrams per cent. This dropped to 6.3 milligrams per cent twenty-four hours after the drug was discontinued. His temperature dropped to normal in the first twenty-four hours of therapy and did not rise again. The only effect noted was the drop of 22 per cent in his hemoglobin and one million in his red count. Similar drops were noted in other cases with a much lower blood concentration. This patient was discharged completely recovered and with a normal blood count.

We found the blood concentration when rectal therapy was used to be approximately half that of the orally treated cases. These patients so treated had a normal temperature in twenty-four hours, two in forty-eight hours, and one which had a Type VI pneumonia engrafted on a tuberculous background had a long and stormy course. Table 10 shows the minimum and maximum concentrations of the seven cases treated per rectum, the time required for the temperature to reach normal, and a comparison in one case of the blood concentrations on analogous days between the two methods of administration. In this particular case, because the temperature did not drop and resolution did not occur, treatment was continued for two successive periods of nine days each. (See Case 7 of Table 10.)

We are convinced we do not know the optimum blood concentration. With the present drug and method of administration we have no way of controlling the degree of concentration. It would seem that it is not necessary to have high concentrations to occasion effective results. One case showing a Type XII blood stream infection had only a trace of the drug in the blood at any time; yet the temperature was normal in twenty-four hours.

CHANGES IN THE BLOOD

While average white counts have little meaning, we quote the following averages in order to show the effect of the drug on the white blood cells. The average count at the beginning of treatment was 23,500 with 80 per cent neutrophils. When treatment was stopped the average count was 10,500 with 65 per cent neutrophils. On discharge the average count had dropped to 9,400 and 66 per cent neutrophils. We concluded that this drop in blood count to normal associated with a return to normal temperature indicated that active infection was at an end. There was no relationship, however, with this drop in the white blood cells and resolution of the pneumonia.

There were other blood changes about which we were not so happy. These adverse effects on the blood cells were the most common unfavorable findings noted with the use of sulfapyridine. Some were mild, others were alarming. They seemingly had no relationship to the amount of the drug given or to the length of time it was administered. These changes are outlined in Table 11.

Leukopenia, ranging from 2,300 to 4,800, occurred in ten cases or 8 per cent. In no case did this require stopping the drug. The effect of treatment was accomplished when the leukopenia appeared. One infant, 15 months old, developed a leukopenia of 4,600 one week after the drug had been discontinued. This followed four days of treatment with a total dosage of 90 grains. These low counts rapidly returned to normal without treatment.

Four cases started therapy with a white count ranging from 5,200 to 7,800. In each case there was rise in this count during the course of the dis-

TABLE 11.—*Blood Changes*

	No.	Per Cent Total Cases	Anemia Before Therapy					
			Low Hemoglobin			Low Red Blood Cells		
			No.	Changes	Per Cent	No.	Changes	Per Cent
Reduction of hemoglobin only								
Major *	15	12 } 40 per cent	16	4	25			
Minor †	35	28 }						
Reduction of red blood cells only								
Major ‡	24	19 } 42 per cent				9	4	44
Minor §	29	23 }						
Reduction of hemoglobin and red blood cells	18	14	7	7		7	7	
Leukemoid reaction ¶	1	0.8						
Leukopenia	10	8						

* More than 15 per cent.
† Less than 15 per cent.
‡ More than 500,000.
§ Less than 500,000.
¶ Journal Pediatrics, Vol. 15:5,740, 1939.

ease and administration of the drug. Temperature in these cases did not drop to normal in a single instance in twenty-four hours. It required forty-eight hours in two cases, three days in another and six days in still another. Two of these cases showed no typing of the sputum.

There were significant changes (more than 15 per cent hemoglobin and 500,000 red blood cells) in the red cells and hemoglobin in thirty-nine cases or 31 per cent. Fifteen cases, or 12 per cent, had a drop in the hemoglobin ranging from 15 to 45 per cent. Twenty-four cases, or 19 per cent, had a drop in the red count ranging from 500,000 to 2,200,000. One was so dramatic and sudden that emergency blood transfusions were necessary. Thirty-five other cases, or 28 per cent, had minor reductions in the hemoglobin or red blood cells. Thus seventy-four cases, or 58 per cent, had reductions in the hemoglobin or red blood cells or both of sufficient degree to note.

Of the thirty-nine cases showing major reduction in the red blood cells and hemoglobin, twenty-five, or 65 per cent, had a hemoglobin below 60 per cent and a red count below 3,750,000 at the start of treatment. It was this group of anemic individuals that was most affected by the drug. In this group there were sixteen cases which started treatment with a low hemoglobin, yet four, or 25 per cent, had severe reductions. Of nine cases which had a low red count when treatment was started, four, or 44 per cent, had severe reductions. Thus it would seem that those patients which have an anemia at the beginning of treatment offer a special hazard when sulfapyridine is used.

We have already published [1] one blood reaction that was strange and severe. This was in a 9-year-old Mexican boy who had a severe Type I pneumonia with a Type I bacteremia. He received the usual dosage. His temperature returned to normal in twenty-four hours. Treatment was stopped after three days. Two days later there was lassitude, temperature of 102 degrees Fahrenheit, marked pallor and slight icterus. In twenty-four hours the red cells dropped from 3,240,000 to 1,380,000 and the hemoglobin from 60 per cent to 22 per cent. The white count increased to 81,000 and showed a leukemoid shift with 22 per cent myelocytes. After several blood transfusions this boy was discharged, five weeks after entry, fully recovered and with a normal blood count. During the time of his acute reaction he had a hemoglobinuria lasting two days.

URINARY CHANGES

Urinary changes were as a rule not significant. Some abnormal condition as shown in Table 12 was noted in twelve cases. But in seven of these the casts, albumin and white blood cells that were found, might have been due to the pneumonia. Free hemorrhage was seen in four cases, or 3 per cent. One of these was quite severe, occurring over a period of several hours. All hemorrhage stopped on the withdrawal of the drug and no aftermath was noted. None were severe enough to warrant transfusions or treatment for an anemia. In one case the hemorrhage was preceded by severe abdominal pain of several hours' duration. Needle-like crystals of acetyl sulfapyridine were seen in the urine of one of these hemorrhage cases. The hemoglobinuria which occurred with the leukemoid reaction has already been mentioned.

SYMPTOMATIC REACTIONS

Symptomatic reactions as shown in Table 13 were rare. Nausea and vomiting were noted in eight cases, two of which were severe enough to warrant stopping the drug. No case receiving the drug per rectum vomited. Mental confusion was present in eight cases. This ranged from mental apathy to ex-

TABLE 12.—*Urinary Changes*

	Number	Per Cent
Hemorrhage	4	3
Casts and albumin	3	2.4
Hemoglobin	1	0.8
Acetylsulfapyridine crystals	1	0.8
White blood cells	4	3

TABLE 13.—*Symptomatic Reactions to Drug*

Reaction	Number	Per Cent
Nausea and vomiting	8	6.3
Mental confusion	5	3.9
Cyanosis	3	2.4
Restlessness	3	2.4
Anorexia	1	0.8
Muscular twitching	1	0.8

treme restlessness, marked disorientation and irrationalism. These conditions rapidly disappeared on withdrawal of the drug. Muscular twitching, associated with extreme restlessness and mental confusion, was of such severity in a child one year old that the drug was discontinued before the temperature reached normal. Cyanosis was noted in only three cases. This symptom did not seem to be as common as in those children receiving sulfanilamide. Extreme anorexia was noted in one case.

COMPLICATIONS OF THE DISEASE

The complications which developed with the disease are shown in Table 14. Five cases developed empyema. Two of these had definite evidence of pleural irritation on entry to the hospital. Both had Type I pneumococcus in the sputum and in the pleural exudate. One of the two had a positive Type I blood culture. Another patient, whose sputum and blood showed no type, presented some questionable pleural involvement on entry. This pleural exudate also showed Type I pneumococcus. Sulfapyridine had no effect on the development or course of the empyema.

One other empyema was due to a hemolytic streptococcus. This case had no sputum type or blood culture. Diagnosis was a diffuse bronchopneumonia. Sulfapyridine was given by rectum for one week. There was a gradual decline in temperature to normal. When the drug was stopped the chest was clinically clear. After remaining well for one week, a definite consolidation occurred in the left upper lobe. Sulfapyridine was again started by mouth but with no effect. Empyema developed rapidly.

Another 9-month infant had a right upper lobe consolidation. Sputum showed Type VII and blood showed Type I pneumococcus. Because of the severe anemia and poor nutritional state, a blood transfusion was given before the sulfapyridine was started. There was no response to the drug even though continued for eight days. It was stopped because of the severe anemia. The blood concentration ranged from 2.2 to 4.8 milligrams per cent. Blood cultures continued positive for two weeks. By the third week x-ray showed almost complete resolution of the lung but with a slight pleural exudate. With the disappearance of the blood stream infection the high fever became low grade. The pleural effusion gradually increased until rib resection was done. The exudate showed Streptococcus viridans and Staphylococcus aureus. All five cases of empyema made an uneventful recovery after surgery.

TABLE 14.—*Complications of Disease*

	Number	Per Cent	Fatality
Empyema	5	5	0
Otitis media	4	3.1	0
Bacteremia	8	6.3	1
Lung abscess	1	0.8	0
Total	18	15.2	1

One 3-year-old boy developed a lung abscess. The right upper lobe consolidation was due to a Type XXIII pneumococcus. Blood cultures were negative. The temperature dropped to normal in twenty-four hours, where it remained for eight days. During this period no change was noted in the consolidation. X-ray eventually demonstrated a cavity in the midst of the consolidation. No culture was obtained from the cavity. Recovery was complete with symptomatic treatment in three months.

MORTALITY

The only death in our series was that of a 9-month Mexican infant, sick for five days before entering the hospital. He was extremely toxic, cyanotic and dyspneic. The sputum did not type, but the blood culture showed Type XII pneumococcus. The child died less than forty-eight hours after therapy was started. No beneficial effects of the drug were noted after 52 grains had been given. The blood concentration was 8.6 milligrams per cent on the first day of treatment and 13.5 milligrams per cent on the day of death. The urine was negative. This one death gives the remarkable death rate of only 0.8 per cent.

SUMMARY

This paper represents a study of 126 cases of pneumonia in children under fourteen years treated with sulfapyridine at the Los Angeles County General Hospital from March through December of 1939. Ninety-nine of the total number of cases were lobar pneumonias and the remaining twenty-seven bronchopneumonias.

Criteria for sulfapyridine therapy were established arbitrarily as follows: (1) clinical diagnosis of severe, toxic pneumonia; (2) x-ray confirmation of physical diagnosis; (3) blood count; (4) urinalysis; (5) blood culture, and (6) sputum typing. Once the drug had been started the routine was (1) daily chest examination; (2) complete hemogram every twenty-four to forty-eight hours during the period of sulfapyridine administration and every three days thereafter; (3) urinalysis every three or four days; (4) check x-ray one week after the temperature had reached normal if the lungs were clinically clear, and (5) sulfapyridine blood concentration daily at the same hour.

Dosage of the drug was calculated on the basis of 1 to 1.5 grains per pound of body weight, the daily dose not to exceed 90 grains in any twenty-four-hour period. The total dose was divided by six and given at four-hour intervals day and night, the initial amount being double the calculated four-hour dose.

The length of time of drug administration varied from two to twelve days. Eighty-three per cent of the total number did not receive the drug longer than five days.

The time required for the temperature to reach normal varied. In 84 per cent of the cases normal temperature was reached in forty-eight hours; in 59 per cent of the total cases this occurred in the first twenty-four hours. Cases requiring longer than six days usually had some complication which the drug did not affect. It is interesting to note that 31 per cent (thirty-nine cases) had subnormal temperatures which persisted for several days.

The blood concentration of the drug was unpredictable. It varied from a trace to a high of 17.9 milligrams per cent. No explanation is offered for this variability. When the drug was given rectally we found the blood concentration to be about half that of the orally treated cases.

Complications of the drug and the disease are discussed at some length.

Mortality for the entire series is 0.8 per cent.

CONCLUSIONS

With the experiences gained in this study we feel justified in drawing the following conclusions:

1. Sulfapyridine is a very effective drug that should be used in every clearly defined pneumococcic pneumonia in children.
2. It is reasonable to expect that sulfapyridine or related compounds will replace all other methods of routine treatment in the pneumococcus pneumonias in pediatrics practice.
3. The routine use of sulfapyridine in clearly defined pneumococcic pneumonias in childhood should markedly reduce the present death rates in this disease.
4. Sulfapyridine is a toxic and dangerous drug especially affecting the blood, blood-forming organs and the kidneys. Every case in which the drug is used is fraught with potential difficulties which may come with alarming suddenness and severity.
5. The drug should never be used unless the patient is completely under the control of the physician who should resort to frequent blood counts and urinalyses.
6. The drug should not be continued over long periods.
7. The drug apparently does not hasten the time of complete resolution and may even slightly retard it.
8. When treated early with sulfapyridine, the lobar pneumonias do not seem to progress on to the massive consolidation so frequently seen in the untreated case.
9. Routine determination of blood concentration is not necessary since no definite level can be established.
10. The degree of blood concentration seemingly has little effect on the speed with which the drug acts or with its ultimate effectiveness.

829 South Alvarado Street.
1200 North State Street.

REFERENCE

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POLYPOID BRONCHIAL TUMORS*

WITH SPECIAL REFERENCE TO BRONCHIAL ADENOMATA

By ALFRED GOLDMAN, M.D.
San Francisco

POLYPOID bronchial tumors are those neoplasms which grow as projections within the bronchial lumen and are visible through the bronchoscope. Until a short time ago, all invasive polypoid bronchial tumors were believed to be malignant. Recently,[1,2] however, polypoid bronchial adenomata have been separated, clinically and pathologically, from the other polypoid tumors, to form a new clinical entity—a polypoid bronchial tumor which, though locally invasive, rarely metastasizes and can be cured.

TYPES OF POLYPOID TUMORS

Since bronchial adenomata are polypoid in form, though nonmetastasizing, and comprise some 6 per cent[3] of all bronchial tumors, it becomes important to classify polypoid tumors in order to select the proper therapy. Three types may be distinguished, namely:

Metastasizing polypoid tumors (carcinoma).

Locally invasive, but nonmetastasizing polypoid tumors (adenoma).

Noninvasive, nonmetastasizing, purely local polypoid tumors (fibroma, lipoma, myoma, and so forth).[4]

The importance of this reclassification, and the recent separation of adenomata from carcinomata, are demonstrated by a review of some of the publications which resulted from their confusion. It seems most probable that certain reports of the successful removal of carcinoma of the lung by means of the bronchoscope,[5-9] and of the cure of carcinoma of the lung by pneumonectomy,[10-13] or deep x-ray therapy,[14,15] actually refer to cases of adenoma.

The various names by which the clinical entity now termed "bronchial adenoma" has been designated have added still further to the confusion. Geipel,[16] in 1931, termed these tumors "basal-cell cancer"; Wessler[2] (1932), "benign bronchial adenoma"; Kernan[17] (1935), "carcinoid"; Moersch[8] (1935), "adenocarcinoma"; Clerf and Crawford[18] (1936), "benign glandular tumors"; Zamora and Schuster,[19] (1937), "vascular adenoma"; Welt and Weinstein,[20] (1937), "endothelioma"; and, finally, Womach and Graham[21] (1938), "mixed tumors of the lung." Yet, undoubtedly, each of these authors referred to the same type of tumor.

RELATION TO AGE AND SEX

The age of the patient at the onset of symptoms of adenoma is strikingly different from that of

* From the Department of Surgery, Division of Thoracic Surgery, University of California Medical School (services of Harold Brunn, M. D., at the University of California and San Francisco hospitals), and from the Department of Public Health, San Francisco Hospital.

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